



PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference HSM-LUP-937 | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEAA416) | |
| International application No. PCT/IN 03/00345 | International filing date (day/month/year) 27.10.2003 | Priority date (day/month/year) 29.10.2002 |
| International Patent Classification (IPC) or both national classification and IPC C07D501/36 | | |
| Applicant LUPIN LIMITED et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

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| Date of submission of the demand 24.05.2004 | Date of completion of this report 02.02.2005 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Grassi, D Telephone No. +49 89 2399-8499  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/N 03/00345

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-18 |
| | No: Claims | 19 |
| Inventive step (IS) | Yes: Claims | 1-18 |
| | No: Claims | 19 |
| Industrial applicability (IA) | Yes: Claims | 1-19 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IN 03/00345

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-26 as originally filed

Claims, Numbers

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
 - ☐ the claims, Nos.:
 - ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IN 03/00345

1) Reference is made to the following documents:

D1: US-A-4937330

D2: Chemical Abstracts, Accession No. 2001:606938 (Zhu et al., Zhongguo Yiyao Gongye Zazhi, "Synthesis of ceftiofur" (2001), 32(6), 241-242)

- 2) The subject-matter of present claims 19 is not new (Article 33(2) PCT).
In example 2 of D1 (see also claim 3) the HCl salt of ceftiofur is neutralized with PVP in aqueous THF and filtered to give the free amine (or free acid) in aqueous THF. The said solution is then added to an excess of sodium-ethyl hexanoate in aqueous THF. In view of the fact that sodium-ethyl hexanoate is the reactant and can also be regarded as organic base, the subject-matter of present claim 19 is not novel (the claim 19 does neither specify that the organic base is different from sodium-ethyl hexanoate nor that the transformation is a two-step procedure).
- 3) The subject-matter of present claims 1-18 is new (Article 33(2) PCT; cf. below).
- 4) The subject-matter of claims 1-18 involves an inventive step (Article 33(3) PCT).

D2 represents the closest prior art and discloses the preparation of ceftiofur from the same starting materials as the present application.

The present claim 1 differs from the process of D2 in that the reaction medium comprises water.

The technical problem underlying the present application is seen in the provision of an improved method for manufacture of ceftiofur (cf. page 1, lines 3/4, of the application).

In view of the fact that the applicant has submitted comparative data showing that the claimed process represents an improvement over D2, inventive activity can be acknowledged (letter of 15.10.04).